The importance of cerebral magnetic resonance imaging in evaluation of neonatal seizures

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into play to determine the child's eventual outcome. Complex environmental factors feed into eventual outcomes following ABI. Future research using the methodologies demonstrated by Kelly et al. should, in my opinion, focus on these variables, creating research projects exploring the effects of focused interventions on this broader environmental process. It is likely that this approach will yield optimal outcomes for the child and his or her family.

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The importance of cerebral magnetic resonance imaging in evaluation of neonatal seizures

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This commentary is on the original article by Weeke et al. on pages 248–256 of this issue.

The diagnosis, evaluation, and management of neonatal seizures remain very challenging areas of neonatology and the outcome is strongly influenced by the underlying cause. The importance of neuroimaging in neonatal seizures has been appreciated for several years, and advances in magnetic resonance imaging (MRI) techniques have contributed to identification of an underlying aetiology and prediction of prognosis in many infants.

However, there are no evidence-based guidelines for the evaluation of neonatal seizures, and suggestions for diagnostic algorithms are scarce in the literature. A recent prospective study has suggested a practical work-up guideline to determine an aetiological diagnosis in neonatal seizures. This study included 221 term neonates with seizures who were admitted to the neonatal intensive care unit of the University Medical Center, Groningen, the Netherlands. Seizure aetiology was investigated by means of a standardized evaluation which was divided into basic and extended components. Basic evaluation was considered mandatory, including history, clinical examination, laboratory work up based on the early detection of the most common and treatable causes of neonatal seizures (e.g. hypoglycemia and infection), cranial US (cUS), and amplitude integrated EEG (aEEG). Even though small intracranial haemorrhages and infarctions may be missed, the algorithm proposed that MRI be part of the extended evaluation, to diagnose congenital malformations of the central nervous system.[1]

In contrast, the recent large retrospective study of Weeke et al. concludes that MRI always makes an important contribution to the diagnosis of neonatal seizures. The authors demonstrated the diagnostic value of cerebral MRI in 354 infants with neonatal seizures. Similar to previous studies, the most common aetiologies of neonatal seizures, were hypoxic-ischaemic encephalopathy, intracranial haemorrhage, and perinatal arterial ischaemic stroke. Most importantly, they found that cUS alone would have made a diagnosis in only 37.9% (134/354) of patients, and that in almost half of the study population, MRI showed additional information that led to more focused diagnostic testing, more accurate prognosis, or appropriate genetic counselling.[2] Thus, while this study clearly adds to the literature on the subject, the problem is that access and availability of neonatal MRI is limited in many institutions, and technically not all institutions can perform MRI studies as promptly (within a week of seizure onset) as was performed in the reported study population.

Furthermore, neonatal seizure detection and monitoring are challenging as both under-recognition and over-diagnosis occur frequently. Clinical detection of neonatal seizures is unreliable and misdiagnosis is extremely common. Continuous video-EEG remains the criterion standard for neonatal seizure detection and quantification, but this is also not widely available and is very labour-intensive.[3] However, aEEG detects up to 90% of neonatal seizures and can result in improved real-time diagnosis and treatment of neonatal seizures.[4]

In our opinion, the design for future studies should aim to integrate new high standard MRI technologies, with detailed and standardized electroclinical correlation as recommended by a consensus of experts who established a systematic neonatal EEG nomenclature, aiming at facilitating collaborative research.[5]

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The puzzling search for neural correlates of performance

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The continuous innovation and refinement of neuroimaging techniques has enabled the quantification of the brain microstructure and functional network development in vivo that were previously not detectable on conventional magnetic resonance imaging (MRI). As of now, a number of brain structures and activity fluctuation patterns have been identified as important underlying mechanisms of function and dysfunction. Advanced MRI techniques are particularly appealing for studying disorders in which specific gene anomaly or brain insult has not yet been identified. These techniques are particularly suited to exploring the neural correlates of neurodevelopmental disorders for which the etiology is, in many cases, thought to be the result of complex interactions between multiple gene expressions of small effect and environmental factors.[1]

Several neurodevelopmental disorders are known to present in comorbidity, resulting in heterogeneous clinical presentations, which frequently include an assortment of motor, attention, and behavioral difficulties. Despite the increasing interest in studying comorbid neurodevelopmental disorders, the relationship between motor and attention deficits remains poorly understood. There is a high incidence of overlapping symptoms between attention-deficit–hyperactivity disorder (ADHD) and developmental coordination disorder (DCD). Years of neuroimaging studies in the ADHD population have shed light on a number of structural brain and activation pattern differences when compared with typically developing peers. Although some of the central nervous system alterations described are part of the known motor pathways and therefore could intuitively explain both the attention and the motor difficulties frequently observed in individuals with ADHD, there is in fact very little concrete evidence on how these neural correlates are specific to motor performance in this population.[2]

Currently, very few studies have comprehensively examined structure-function relationships in these complex neurodevelopmental disorders, whether it is in their isolated or comorbid form. In their new study, Langevin et al.[3] uniquely report group-specific associations between areas of cortical thinning and decreased performance on motor and attentional standardized evaluations. Although these preliminary findings need further validation in larger samples, which would enable the ability to control for more confounders, the authors made a significant attempt to increase the clinical relevance of their findings in correlating neural substrates with performance measures. These associations should nonetheless be interpreted with caution as lower performance does not unconditionally translate to impairment.

Studying the developing brain is extremely challenging because of its plasticity and the seemingly infinite number of factors that are likely to influence growth trajectory. Early life experiences (i.e. pain, neonatal illness) have been shown to affect cerebral development in preterm infants,[4] a group particularly at risk to later present with ADHD and/or DCD. More than the critical period surrounding birth, other events during childhood are also likely to shape the brain's developmental trajectory. For instance, ante/perinatal factors as well as environmental factors during early development have been suggested to differently contribute to the presentation of ADHD profiles.[5] Moreover the use of stimulant medication, the most common treatment for ADHD, seems to normalize brain structure and activity when compared with unmedicated individuals with the disorder.[6] It becomes extremely difficult to control for these variables in cross-sectional designs of samples recruited during childhood and adolescence. It is only with the very challenging implementation of large longitudinal investigations using serial neuroimaging during the neonatal period